Background on BSE

Bovine spongiform encephalopathy (BSE), widely known as "mad cow disease," is a chronic, degenerative disease affecting the central nervous system of cattle. Worldwide there have been more than 180,000 cases since the disease was first diagnosed in 1986 in Great Britain. BSE has had a substantial impact on the livestock industry in the United Kingdom. The disease has also been confirmed in native-born cattle in Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Israel, Italy, Japan, Luxembourg, Liechtenstein, the Netherlands, Northern Ireland, Poland, Portugal, Slovakia, Slovenia, Spain and Switzerland. However, over 95% of all BSE cases have occurred in the United Kingdom. There have been two confirmed cases of BSE in North America, both from a herd that originated in Canada. One was confirmed in May of 2003 in Alberta Canada while the other was confirmed in an animal found in Washington State in the US in December 2003.

BSE belongs to the family of diseases known as the transmissible spongiform encephalopathies (TSE's). These diseases are caused by a transmissible agent which is yet to be fully characterized. They share the following common characteristics

a. a prolonged incubation period of months or years;
b. a progressive debilitating neurological illness which is always fatal;
c. when examined by electron microscopy, detergent treated extracts of brain tissue from animals or humans affected by these diseases reveal the presence of scrapie associated fibrils (SAF);
d. pathological changes appear to be confined to the CNS and include vacuolation, and astrocytosis;
e. the transmissible agent elicits no detectable specific immune response in the host which has inhibited the development of a preclinical live animal diagnostic test to date.

Clinical Signs of BSE in Cattle

Affected animals may display changes in temperament, such as nervousness or aggression; abnormal posture; incoordination and difficulty in rising; decreased milk production; or loss of body condition despite continued appetite. There is no treatment, and affected cattle die.

The incubation period ranges from 2 to 8 years. Following the onset of clinical signs, the animal's condition deteriorates until it dies or is destroyed. This usually takes from 2 weeks to 6 months. Most cases in Great Britain have occurred in dairy cows between 3 and 6 years of age.

How BSE Is Currently Diagnosed

There is no test to detect the disease in a live animal. Currently there are two laboratory methods to confirm a diagnosis of BSE: 1. microscopic examination of the brain tissue to identify characteristic changes; 2. techniques to detect the partially-proteinase resistant form of the prion (PrP^{res}) protein. These techniques are immunohistochemistry, immunoblotting and ELISA.

Similar Diseases of Humans and Other Animals

TSE's are caused by similar uncharacterized agents which usually produce spongiform changes in the brain. TSE's include scrapie (which affects sheep and goats), transmissible mink encephalopathy, feline spongiform encephalopathy, chronic wasting disease of deer and elk, and in humans, kuru, Classical Creutzfeld-Jakob Disease (CJD), Gerstmann- Straussler syndrome, fatal familial insomnia, and vCJD.

BSE and vCJD—Human Health Concerns

On March 20, 1996, the UK's Spongiform Encephalopathy Advisory Committee (SEAC) announced the identification of 10 cases of a new variant form of CJD (vCJD). All of the patients developed onset of illness in 1994 or 1995. The following features describe how these 10 cases differed from the sporadic form of CJD:

- The affected individuals were much younger than the classical CJD patient. Typically, CJD patients are over 63 years old. The average patient age for the onset of variant CJD was 28 (range of 12 to 74) years.
- The course of the disease in the vCJD averaged 14 months. Classical CJD cases average a 4–6 month duration.
- In the variant cases, electroencephalographic (EEG) electrical activity in the brain was not typical of classical CJD.
- Although brain pathology was recognizable as CJD, the pattern was different from sporadic CJD, with large aggregates of prion protein plaques.

Epidemiological and case studies have not revealed a common risk factor among the cases of vCJD. According to the SEAC, all victims were reported to have eaten beef or beef products in the last 10 years, but none had knowingly eaten brain material. One of the affected individuals had been a vegetarian since 1991.

The SEAC concluded that although there was no direct scientific evidence of a link between BSE and vCJD, based on current data and in the absence of any credible alternative, the most likely explanation at that time was that the cases were linked to exposure to BSE before the introduction of control measures, in particular, the specified bovine offal (SBO) ban in 1989.

Research reported in later 1996 and 1997 has found evidence to further support a causal association between vCJD and BSE. Two significant studies published in the October 2, 1997 edition of *Nature* lead the SEAC to conclude that BSE agent is highly likely to be the cause of vCJD. Dr. Moira Bruce and colleagues at the Institute for Animal Health in Edinburgh, Scotland inoculated 3 panels of inbred mice and one panel of crossbred mice with BSE, vCJD and sporadic CJD. Results indicate that mice inoculated with BSE showed the same pattern of incubation time, clinical signs and brain lesions as mice inoculated with tissues from patients with vCJD. This provides evidence that BSE and vCJD have the same signature or are the same "strain". In addition, sporadic CJD and known scrapie strains were not similar to vCJD or BSE.

Results from a study published by Dr. John Collinge and colleagues of Imperial College School of Medicine, London, UK strongly support Bruce's results. Collinge's paper reports findings of BSE transmission to transgenic mice expressing only human PrP.

Another paper by Collinge et al. in the October 24, 1996 edition of *Nature* also provides data to support the association between vCJD and BSE.

More recently, studies using transgenic animals expressing the bovine PrP have supported the view that BSE infected cattle are responsible for vCJD. These mice not only propagated the BSE infectious agent in the absence of a species barrier, but also were highly susceptible to vCJD. Furthermore, the transgenic mice inoculated with either vCJD or BSE had indistinguishable disease characteristics.

Where has vCJD been Detected?

The variant form of CJD has been detected in the United Kingdom. The UK CJD Surveillance Unit provides a monthly update. There have also been 6 cases of vCJD in France, 1 in Ireland, and 1 probable case in the United States and Italy.

On April 18th, 2002, the Florida Department of Health and the CDC reported a likely case of new variant Creutzfeldt Jakob disease (vCJD) in a 22-year-old citizen of the United Kingdom living in Florida. The clinical diagnosis was recently made at a hospital in the U.K. and she has since returned to the U.S. Information provided by the U.K. indicates that the patient's clinical condition and history are consistent with vCJD acquired in the U.K. However, the only way to confirm a diagnosis of vCJD is through study of brain tissue obtained by a brain biopsy or at autopsy.

New variant CJD is a rare, degenerative, fatal brain disorder that emerged in the U.K. in the mid-1990s. Although experience with this new disease is limited, evidence to date indicates that there has never been a case transmitted from person to person. Rather, the disease is thought to result from consumption of cattle products contaminated with an agent that causes a disease called bovine spongiform encephalopathy (BSE, commonly known as mad cow disease). To date, no case of this cattle disease has been identified in the United States by the USDA.

If confirmed, this would be the first case of vCJD reported in a U.S. resident. However, because the disease is thought to have a long incubation period, CDC believes the patient acquired the disease while living in the U.K.

For more information, please visit the CDC web site or the Florida Department of Health Web site.

Transmission of BSE

There is no evidence that BSE spreads horizontally, i.e., by contact between unrelated adult cattle or from cattle to other species. Some evidence suggests that maternal transmission may occur at an extremely low level. Results of British research show that there is approximately a 9-percent increase in the occurrence of BSE in offspring of BSE-affected dams as compared to calves born to dams where BSE was not detected. The study did not ascertain if this was the result of genetic factors or true transmission. The research did however point out that at this level if maternal transmission does occur it alone will not sustain the epidemic (Wilesmith et al. 1997).

A recently published study found no evidence of disease transmission via embryos collected from cows with BSE. The embryos were collected and handled in accordance with international health standards (Wrethall et al., 2001).